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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/359,326 07/20/99 REITER

R. 30435.54US14

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HM22/0612

EXAMINER

HELMS, L

ART UNIT	PAPER NUMBER
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1642

17

DATE MAILED:

06/12/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.  
09/359,326

Applicant(s)

Reiter et al

Examiner  
Larry R. Helms Ph.D.

Art Unit  
1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 17 Apr 2001
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 18-86 is/are pending in the application.
- 4a) Of the above, claim(s) 18-86 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 69-86 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☒ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3 and 15 20) ☐ Other: \_\_\_\_\_

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### **DETAILED ACTION**

1. Claims 1-3, 7, 18-86 are pending. **NOTE:** newly submitted claims 18-35 have been renumbered as 69-86, respectively, under Rule 126.

Claims 4-6, 9-17 have been canceled.

Claims 1-3 have been amended.

2. Claims 18-68 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

3. Claims 1-3 and 69-86 are under examination.

4. The text of those sections of title 35, USC Code not included on the Office Action can be found in a prior Office Action.

5. The following Office Action contains some NEW GROUNDS of rejection.

### ***Oath/Declaration***

6. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

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The oath claims benefit under USC 120 to U.S. Application 09/308,503. The correct application should be 09/318,503. In addition, the oath does not indicate if priority is claimed under USC 119(e) for provisional applications 60/120,536 or 60/228,816.

Appropriate correction is required.

***Rejections Withdrawn***

7. The rejection of claims 4 and 5 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

8. The rejection of claims 1-5, 9-11 under 35 U.S.C. 102(e) as being anticipated by Au-Young (U.S. Patent 5,856,136, filed 7/3/96) is withdrawn in view of the amendment to the claims.

***Response to Arguments***

***Priority***

9. The examiner acknowledges the statements concerning priority on pages 20-22 and pages 26-30 of the response filed 4/17/01. Upon review of these statements the following priority dates are granted to the claims.

Claims 1, 3     3/98

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Claim 2        12/98   no teaching of "middle portion" in 09/038,261. Only C-terminal and N-terminal.

Claim 69-70   12/98 due to dependancy on claim 2.

Claims 71-72   7/99 no teaching of "human" antibody in 09/251,835. Only "humanized antibody" at page 23, lines 27-29.

Claim 73       2/99 due to arguments on page 29 of response.

Claim 74       12/98 due to dependancy on claim 2.

Claims 75-80   12/98 due to dependancy on claim 2.

Claims 81 and 86    7/99 due to no support in prior applications for "ricin-A-chain" and arbrin A chin...sapaonaria officinalis inhibitor" as recited in these claims. Only support is found in the instant application at page 31, lines 1-7.

Claim 82 and 83    12/98 due to dependence on claim 2.

Claim 84       7/99 due to statement on page 22 of response with support on page 31, lines 7-8 of the instant application.

Claim 85       12/98 due to the dependence on claim 2.

***Double Patenting***

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10. The rejection of claims 1-3 and newly submitted claim 74 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 12-13 of copending Application No. 09/203939 is maintained.

The response filed 4/17/01 has been carefully considered but is deemed not to be persuasive. The response states "Upon an indication of allowability [ ] applicants will provide a terminal disclaimer" (see page 30 of response). No terminal disclaimer has been filed and as such the rejection stands.

***Claim Rejections - 35 USC § 103***

11. The rejection of newly added claims 71 and 72 under 35 U.S.C. 103(a) as being unpatentable over Au-Young (U.S. Patent 5,856,136, filed 7/3/96) and further in view of Green et al (Nature Genetics 7:13-21, 1994) is maintained and made again.

The response filed 4/17/01 has been carefully considered but is deemed not to be persuasive. The response states that "Green fails to teach or suggest human monoclonal antibodies which bind PSCA" (see page 34 of response). In response to this argument, Au-Young clearly teaches monoclonal antibodies to PSCA and these antibodies can be produced in vivo in a lymphocyte population as demonstrated by the method of Green et al which teach any antigen can be used to immunize the mouse to produce fully human immunoglobulins.

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12. The rejection of claims 1-3, and newly submitted claims 77, 80-82, and 85-86 under 35 U.S.C. 103(a) as being unpatentable over Au-Young (U.S. Patent 5,856,136, filed 7/3/96) and further in view of Thorpe et al (Immunological Rev. 62:119-158, 1982) is maintained.

The response filed 4/17/01 has been carefully considered but is deemed not to be persuasive. The response states "Thorpe fails to teach or suggest antibodies directed to specific portions of PSCA that are conjugated to a cytotoxic agent" (see page 35). In response to this argument against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In addition, Au-Young teach the antibodies are used in therapy for tumors and it would be obvious in view of Thorpe to produce a cytotoxic agent conjugated to the antibody of Au-Young to target the tumor.

*The following are some NEW GROUNDS of rejections*

***Claim Rejections - 35 USC § 112***

13 Claims 1-3, 69-86 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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a. Claims 1-3 and 69-86 are indefinite for reciting “or a portion thereof” in claims 1-3 because the exact meaning of the phrase is not clear. Does the phrase mean the antibody binds an amino acid of SEQ ID NO:2, an epitope contained in amino acids of 2-50, 46-109, or 85-123 of SEQ ID NO:2, etc?

b. Claim 69 is indefinite for reciting “chimeric” as the exact meaning of the word is not known. The term chimeric is generic to a class of antibodies which are products of genetic shuffling of antibody domains and other active proteins. The term encompasses antibodies fused to non-immunoglobulin proteins as well as antibodies wherein any domain of the antibody is substituted by corresponding regions or residues of human antibodies including but not limited to CDR grafted antibodies. In absence of a single defined art recognized meaning for the phrase and lacking a definition of the term in the specification, one of skill in the art could not determine the metes and bounds of the claims.

c. Claims 79 and 84 are indefinite for reciting “<sup>131</sup>In” because the exact meaning of the term is not clear. It is not clear if <sup>131</sup>In is a radioisotope. Was the term meant to be “<sup>111</sup>In”?

***Claim Rejections - 35 USC § 103***

14. Claims 1-3, 69-70, and 73-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Au-Young (U.S. Patent 5,856,136, filed 7/3/96).

The claims recite a monoclonal antibody which recognizes and binds the C-terminal portion comprising amino acid residues 85-123 of SEQ ID NO:2 or a portion thereof, the N-



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terminal portion comprising amino acids 2-50 of SEQ ID NO:2 or a portion thereof, or middle portion comprising amino acids 46-109 of SEQ ID NO:2 or a portion thereof, the hybridoma producing the antibody, the antibody which is internalized, a recombinant antibody comprising the antigen binding region, a F(ab)<sub>2</sub> fragment, and an antibody comprising murine variable and human constant residues.

Au-Young teach SEQ ID NO:2 which is identical to SEQ ID NO:2 in the instant application. Au-Young also teach antibodies to protein fragments of SEQ ID NO:2 (column 13-14) which are immunogenic and F(ab)<sub>2</sub> fragment (column 14, line 51), and hybridomas producing the antibody (column 14, line 25). Au-Young also teach humanized antibodies (column 14, lines 33-45), recombinantly produced antigen binding fragments (column 14, lines 43-48) and immunoconjugates comprising an antibody and radionuclides (column 12, line 60). Au-Young also teach antibodies compositions are useful for the treatment or prevention of conditions associated with the presence or expression of the antigen (column 2, lines 59-63). Au-Young also teach antibodies can be made to "a portion of the amino acid sequence of the natural protein and may contain the entire amino acid sequence Of[or] a small naturally occurring molecules." (Column 14, lines 1-4). Au-Young teach production of antibodies by determining regions of high immunogenicity and analysis to select epitopes such as those near the C-terminus or in hydrophilic regions as shown in Figure 5 (see column 28, lines 27-38). Au-Young does not teach antibodies to residues 2-50 or a region thereof, residues 46-109 or a region thereof, or residues 85-123 or a region thereof.

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It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced antibodies and antigen binding fragments to residues in the N-terminal, middle, or C-terminal or regions thereof of SEQ ID NO:2 in view of the teachings of Au-Young.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced antibodies and antigen binding fragments to residues in the N-terminal, middle, or C-terminal or regions thereof of SEQ ID NO:2 in view of the teachings of Au-Young because Au-Young teach selecting epitopes or peptides near the C-terminus or in regions that are hydrophilic as shown in Figure 5 for producing antibodies. Thus, it would have been obvious to one skill in the art at the time the claimed invention was made to select regions of SEQ ID NO:2 that are at or near the C-terminus or in a region as shown in Figure 5 which encompass residues recited in the claims, or regions thereof. In addition, it would be obvious that the antibodies are internalized by the cell expressing SEQ ID NO:2.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

15. Claims 76-79 and 82-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Au-Young (U.S. Patent 5,856,136, filed 7/3/96) and further in view of Helstrom et al (U.S. Patent 5,980,896, filed 6/14/96).

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The claims recite an immunotoxin comprising an antibody to regions of SEQ ID NO:2 and 131I.

Au-Young has been described supra. Au-Young does not teach an immunoconjugate of an antibody and 131I. This deficiency is made up for in the teachings of Helstrom et al.

Helstrom et al teaches immunoconjugates of 131I and antibodies for tumor therapy.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an immunoconjugate of the antibody of Au-Young with 131I as taught by Helstrom et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an immunoconjugate of the antibody of Au-Young with 131I as taught by Helstrom et al because Au-Young teach therapy with the antibody directed to SEQ ID NO:2 (see column 22, lines 35-37) and SEQ ID NO:2 has been associated with cancer (see column 4, lines 16-30) and the antibodies will bind the antigen on tumor cells in vivo or in vitro (see column 2, lines 50-52). In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an immunoconjugate of the antibody of Au-Young with 131I as taught by Helstrom et al because Helstrom et al teach an antibody conjugated to 131I for tumor killing . It would be obvious that since SEQ ID NO:2 is associated with cancer and Au-Young teach an antibody directed to regions of SEQ ID NO:2 that one skill in the art would label the antibody with 131I as taught by Helstrom to eradicate the tumor.

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Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

### *Conclusions*

16. No Claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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Respectfully,

Larry R. Helms Ph.D.

703-306-5879

  
SHEELA HUFF  
PRIMARY EXAMINER